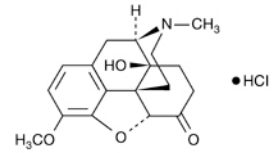
**OXYCODONE AND ACETAMINOPHEN - oxycodone hydrochloride and acetaminophen capsule, gelatin coated**
Mallinckrodt Inc.

**OXYCODONE AND ACETAMINOPHEN**
**CAPSULES USP**
**5 mg/500 mg**
**CII**
**Rx only**
Analgesic For Oral Use

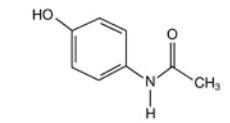
## DESCRIPTION

Each Oxycodone and Acetaminophen Capsule USP 5 mg/500 mg contains:
Oxycodone Hydrochloride USP……5 mg*
Acetaminophen USP..……...500 mg
*5 mg Oxycodone Hydrochloride USP is equivalent to 4.4815 mg oxycodone.
In addition, each capsule contains the following inactive ingredients: gelatin, magnesium stearate, silicon dioxide, sodium lauryl sulfate, pregelatinized starch, stearic acid, FD&C Blue No. 1, FD&C Red No. 40, FD&C Yellow No. 6, and titanium dioxide.
The oxycodone component is 4,5α-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride, a white, odorless, crystalline powder having a saline, bitter taste. It is derived from the opium alkaloid thebaine. Oxycodone hydrochloride may be represented by the structural formula shown below:




$C_{18}H_{21}NO_4 \cdot HCl$ MW = 351.82

Acetaminophen, 4#-hydroxyacetanilide, is a non-opiate, non-salicylate analgesic and antipyretic which occurs as a white, odorless, crystalline powder with a slightly bitter taste. It has the following structural formula:




$C_8H_9NO_2$ MW = 151.16

## CLINICAL PHARMACOLOGY

The principal ingredient, oxycodone, is a semisynthetic narcotic analgesic with multiple actions qualitatively similar to those of morphine; the most prominent of these involve the central nervous system and organs composed of smooth muscle. The principal actions of therapeutic value of the oxycodone in this product are analgesia and sedation.
Oxycodone is similar to codeine and methadone in that it retains at least one-half of its analgesic activity when administered orally.
Acetaminophen is a non-opiate, non-salicylate analgesic and antipyretic.

## INDICATIONS AND USAGE

Oxycodone and acetaminophen capsules are indicated for the relief of moderate to moderately severe pain.

## CONTRAINDICATIONS

This product should not be administered to patients who are hypersensitive to any components.

## WARNINGS

### DRUG DEPENDENCE

Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of this drug, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, oxycodone and acetaminophen capsules are subject to the Federal Controlled Substances Act (Schedule II).

## PRECAUTIONS

### GENERAL

**Head Injury and Increased Intracranial Pressure** – The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing

increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.
**Acute Abdominal Conditions** – The administration of products containing oxycodone or other narcotics may obscure the diagnosis or clinical course of patients with acute abdominal conditions.
**Special Risk Patients** – Oxycodone and acetaminophen capsules should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

**INFORMATION FOR PATIENTS**
Oxycodone may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using oxycodone and acetaminophen capsules should be cautioned accordingly.

**DRUG INTERACTIONS**
Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with oxycodone and acetaminophen capsules may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.
The concurrent use of anticholinergics with narcotics may produce paralytic ileus.

**PREGNANCY**
**Teratogenic Effects.** *Pregnancy Category C* – Animal reproductive studies have not been conducted with oxycodone and acetaminophen capsules. It is also not known whether oxycodone and acetaminophen capsules can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Oxycodone and acetaminophen capsules should not be given to a pregnant woman unless in the judgment of the physician, the potential benefits outweigh the possible hazards.
**Nonteratogenic Effects** – Use of narcotics during pregnancy may produce physical dependence in the neonate.

**LABOR AND DELIVERY**
As with all narcotics, administration of oxycodone and acetaminophen capsules to the mother shortly before delivery may result in some degree of respiratory depression in the newborn and the mother, especially if higher doses are used.

**NURSING MOTHERS**
It is not known whether the components of this product are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when oxycodone and acetaminophen capsules are administered to a nursing woman.

**PEDIATRIC USE**
Safety and effectiveness in pediatric patients have not been established.

**ADVERSE REACTIONS**
The most frequently observed adverse reactions include lightheadedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in non-ambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.
Other adverse reactions include allergic reactions, euphoria, dysphoria, constipation, skin rash and pruritus. At higher doses, oxycodone has most of the disadvantages of morphine including respiratory depression.

**DRUG ABUSE AND DEPENDENCE**
Oxycodone and acetaminophen capsules are a Schedule II controlled substance.
Oxycodone can produce drug dependence and has the potential for being abused (*see* **WARNINGS**).

**OVERDOSAGE**

**ACETAMINOPHEN**
**Signs and Symptoms** – In acute acetaminophen overdosage, dose-dependent, potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubular necrosis, hypoglycemic coma and thrombocytopenia may also occur.
In adults, hepatic toxicity has rarely been reported with acute overdoses of less than
10 grams and fatalities with less than 15 grams. Importantly, young children seem to be more resistant than adults to the hepatotoxic effect of an acetaminophen overdose. Despite this, the measures outlined below should be initiated in any adult or child suspected of having ingested an acetaminophen overdose.
Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diaphoresis and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion.
**Treatment** – The stomach should be emptied promptly by lavage or by induction of emesis with syrup of ipecac. Patients' estimates of the quantity of a drug ingested are notoriously unreliable. Therefore, if an acetaminophen overdose is suspected, a serum

acetaminophen assay should be obtained as early as possible, but no sooner than four hours following ingestion. Liver function studies should be obtained initially and repeated at 24-hour intervals.
The antidote, N-acetylcysteine, should be administered as early as possible, and within 16 hours of the overdose ingestion for optimal results. Following recovery, there are no residual, structural, or functional hepatic abnormalities.

**OXYCODONE**
**Signs and Symptoms** – Serious overdosage with oxycodone is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdosage, apnea, circulatory collapse, cardiac arrest and death may occur.
**Treatment** – Primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonist naloxone hydrochloride is a specific antidote against respiratory depression which may result from overdosage or unusual sensitivity to narcotics, including oxycodone. Therefore, an appropriate dose of naloxone hydrochloride (usual initial adult dose 0.4 mg to 2 mg) should be administered, preferably by the intravenous route, and simultaneously with efforts at respiratory resuscitation (see package insert). Since the duration of action of oxycodone may exceed that of the antagonist, the patient should be kept under continued surveillance and repeated doses of the antagonist should be administered as needed to maintain adequate respiration.
An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.
Gastric emptying may be useful in removing unabsorbed drug.

**DOSAGE AND ADMINISTRATION**
Dosage should be adjusted according to the severity of the pain and the response of the patient. However, it should be kept in mind that tolerance to oxycodone can develop with continued use and that the incidence of untoward effects is dose related. This product is inappropriate even in high doses for severe or intractable pain. Oxycodone and acetaminophen capsules are given orally.
The usual adult dosage is one capsule every 6 hours as needed for pain.

**HOW SUPPLIED**
Each Oxycodone and Acetaminophen Capsule USP contains oxycodone hydrochloride 5 mg (equivalent to 4.4815 mg oxycodone) and acetaminophen 500 mg. It is available as a red/beige hard gelatin capsule imprinted with M 532 identification number.

Bottles of 100……NDC 0406-0532-01

Bottles of 500……NDC 0406-0532-05

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].
Dispense in a tight, light-resistant container with a child-resistant closure.
Protect from moisture.
DEA Order Form Required.

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Mallinckrodt Inc.,
Hazelwood, MO 63042 USA.
Printed in U.S.A.
**COVIDIEN™**
**Mallinckrodt**
Rev 121608

**PACKAGE LABEL - PRINCIPAL DISPLAY PANEL - 5 MG*/500 MG**
**Multiple strengths. Do not dispense unless strength is stated.**
NDC 0406-0532-05
**500 CAPSULES**
**OXYCODONE AND ACETAMINOPHEN CAPSULES USP**
CII
**5 mg*/500 mg**
Each capsule contains:
Oxycodone Hydrochloride USP. . . . . 5 mg*
Acetaminophen USP. . . . . 500 mg
**Rx only**
**Mallinckrodt**


Exp.:
Lot No.:
Multiple strengths. Do not dispense unless strength is stated.
3 0406-0532-05 2
LO0005 Rev 121608
NDC 0406-0532-05
500 CAPSULES
OXYCODONE AND ACETAMINOPHEN
CAPSULES USP
C II
5 mg*/500 mg
Each capsule contains:
Oxycodone Hydrochloride USP..... 5 mg*
Acetaminophen USP ..... 500 mg
Rx only
Mallinckrodt
USUAL ADULT DOSAGE:
See package insert.
Protect from moisture.
Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].
Dispense in a tight, light-resistant container with a child-resistant closure.
*5 mg Oxycodone HCl is equivalent to 4.4815 mg oxycodone.
Do not accept if seal over bottle opening is broken or missing.
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